UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/575,300	09/18/2006	Matthias Ebert	MST-2390.1	3699

7590 10/19/2007

Leona L Lauder
Attorney at Law
Suite 1026
235 Montgomery Street
San Francisco, CA 94104-3008

EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
10/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/575,300	EBERT ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 August 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,14,16 and 18-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11, 14, 16, and 18-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 8/16/07 in response to the Office Action of 5/17/07 are acknowledged and have been entered.

Claims 1-11, 14, 16, and 18-24 are pending.

Claims 1, 2, 8, 14, 21, and 24 have been amended by Applicant.

Claims 1-11, 14, 16, and 18-24 are currently under examination.

Objections Withdrawn

The objections to claims 2 and 24 are withdrawn.

Rejections Withdrawn

The rejection under 35 U.S.C. 101 is withdrawn.

The rejection of claim 8 under 35 U.S.C. 112 second paragraph, for reciting "weak staining", "moderate staining", and "strong staining", is withdrawn.

The rejection of claim 8 under 35 U.S.C. 112 second paragraph, for reciting : "...wherein if the immunoreactivity score of the sample determined in steps b(1) to b(3) is above the average immunoreactivity score of said comparable samples...", is withdrawn.

The rejection of claim 21 under 35 U.S.C. 112 second paragraph, for lacking method steps, is withdrawn.

The rejection of claim 24 under 35 U.S.C. 112 second paragraph, for reciting "...said tissue loses or expresses MN/CA IX at a significantly reduced level upon carcinogenesis...", is withdrawn.

The rejection of claim 24 under 35 U.S.C. 112 second paragraph, for reciting "...a tissue sample from the invasion front of said preneoplastic/neoplastic disease....the level that said MN/CA9 gene expression product is normally expressed in said tissue, when said tissue is unaffected by said disease...", is withdrawn.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 1 under 35 U.S.C. 112 second paragraph, for reciting "poorer prognosis", is maintained for the reasons stated in the Office Action of 5/17/07 and for the reasons set-forth below.

In the Reply of 8/16/07, Applicant argues that the term "poorer prognosis" is conventional in the prognostic art related to cancer and restricting claim 1 to a type or types of poorer prognosis would unduly limit the protection of the invention. Applicant

further states that claims are read in light of the specification, which describes exemplary and preferred prognosis of "shortened survival, increased risk of recurrence of said preneoplastic/neoplastic disease, or...diminished or refractory response to treatment" (see lines 22-25 on page 9 of the specification).

The arguments found in the Reply of 8/16/07 have been carefully considered, but are not deemed persuasive. In regards to the arguments that "poorer prognosis" is conventional in the prognostic art related to cancer and restricting claim 1 to a type or types of poorer prognosis would unduly limit the protection of the invention, it is unclear as compared *to what* said prognosis is "poorer". Further, in regards to the argument that the specification describes exemplary and preferred prognosis of "shortened survival, increased risk of recurrence of said preneoplastic/neoplastic disease, or...diminished or refractory response to treatment", the Examiner is not suggesting that Applicant obviate *this* rejection by reciting a particular type of preferred prognosis (such as shortened survival, increased risk of recurrence of said preneoplastic/neoplastic disease, or...diminished or refractory response to treatment) . However, without reciting as compared to what a prognosis is poorer, the meets and bounds of the claims cannot be determined. To obviate this rejection, Applicant may want to amend claim 1 to incorporate language analogous to that of part "c" of claim 24, which recites a method wherein a subject with a first particular type of expression has a poorer prognosis *than if said subject had a second particular type of expression*.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-11, 14, 16, 18-24 under 35 U.S.C. 112 first paragraph, as failing to comply with the written description requirement, is maintained for the reasons stated in the Office Action of 5/17/07 and for the reasons set-forth below.

The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In the instant case, the claims are inclusive of genera of tissue samples taken from a subject vertebrate with a disease that affects a tissue which normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis (see claims 1 and 24). The written description in this case sets forth gastric cancer tissue samples as samples comprising neoplastic tissue taken from a subject vertebrate with a disease (gastric cancer) that affects a tissue which normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis (see Example 2, in particular). The specification does not disclose and the prior art does not teach the genera of tissue samples taken from a subject vertebrate with a disease that affects a tissue which normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis.

The state of the prior art is such that MN/CA IX expression has been shown to be elevated in a few cancers and reduced in others (such as gastric cancers) (see Bui et al: Clinical Cancer Research, 2/03, 9:802-811). However, the state of the art is such that it is unclear which cancers, other than gastric cancers, result in a decrease in MN/CA IX expression upon carcinogenesis.

In the Reply of 8/16/07, Applicant argues that there is a strong presumption that adequate written description of the claimed invention is present when the application is filed and that the Examiner has not introduced sufficient evidence to shift the initial burden of proof to the Applicants. In regards to genera of tissues which normally expresses MN/CA IX protein, but lose or have significantly reduced MN/CA IX expression upon carcinogenesis, Applicant points to the teachings of Pastorekov and Zavada (Cancer Therapy, 2004, 2:245-262). Pastorekov and Zavada teach that stomach and gallbladder tissues have high natural MN/CA IX expression and lose or reduce MN/CA IX expression upon conversion to carcinomas. Applicant further argues that the claims are drawn to a pioneering invention and that case law clearly indicates that pioneering inventions are entitled to broad claim coverage. In regards to University of Rochester v G.D. Searle Co., Applicant argues that the instant claims differ from those of University of Rochester v G.D. Searle Co in that they concern proteins and/or polypeptides that are specifically bound by a known Mab. In regards to University of California v. Eli Lilly and Co., Applicant indicates that the instant case differs in that the instant claims are drawn to methods and not compositions of matter and are drawn to methods comprising described polypeptides. In regards to Fiers v. Revel, Applicant

indicates that the instant case differs in that the instant claims are drawn to method comprising described polypeptides and do not merely recite functional language. In regards to Amgen inc. v. Chugai Pharmaceuticals, Applicant indicates that the instant case differs in that the instant claims are drawn to method comprising described polypeptides. In regards to Fiddes v .Baird, Applicant indicates that the instant case differs in that the instant claims are drawn to method comprising described polypeptides.

The amendments to the claims and the arguments found in the Reply of 8/16/07 have been carefully considered, but are not deemed to be persuasive in regards genera of tissue samples taken from a subject vertebrate with a disease that affects a tissue which normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis (see claims 1 and 24). In regards to the argument that Examiner has not introduced sufficient evidence to shift the initial burden of proof to the Applicant, the state of the art is such that it is unclear which cancers result in a decrease in MN/CA IX expression upon carcinogenesis. The Reply of 8/16/07 and the teaching of Pastorekov and Zavada indicate that two cancers, stomach (gastric) cancer and gallbladder cancer, have reduced MN/CA IX expression as compared to MN/CA IX expression in normal stomach and gallbladder (page 248 of Pastorekov and Zavada, in particular). Further, the Reply of 8/16/07 and the teaching of Pastorekov and Zavada indicate that MN/CA IX is overexpressed in carcinomas of the cervix, uteri, esophagus, kidney, lung, and breast (see page 248 of Pastorekov and Zavada, in particular). However, based on the disclosure and the art one of skill would

not recognize which cancers other than those of the stomach and gallbladder are encompassed by the genera.

Further, in regards to the argument that the claims are drawn to a pioneering invention and that case law clearly indicates that pioneering inventions are entitled to broad claim coverage, it has not been demonstrated that the claims are drawn to a "pioneering' invention that predictably functions as broadly claimed. The broad coverage to which the pending claims are drawn is predominantly supported by a demonstration that elevated expression of MN/CA IX in a *single species* of cancer (gastric cancer) is indicative of a *single type* of prognosis (shorter survival). Without demonstrating a trend between a particular prognosis and expression levels of MN/CA IX protein in samples from numerous types of diseases comprising preneoplastic/neoplastic tissues taken from subjects wherein the diseases affect a tissue which normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis, one would not predict that all samples comprising preneoplastic/neoplastic tissue taken from a subject with a disease that affects said tissue which normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis, would function as claimed. Further, even if the claims were drawn to a pioneering invention, the claims would not be exempt from 35 U.S.C. 112, first paragraph.

In regards to the argument that that instant claims differ from case law cited in the Office Action of 5/17/07 in that they concern method claims and proteins and/or polypeptides that are specifically bound by a known Mab, the genus of MN/CA IX

proteins and/or polypeptides of the claimed invention has been adequately described due to amendments to the claims and is no longer part of this rejection. However, the claimed genera of samples from subjects with a disease that affects a tissue which normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis, are not adequately described because of the reasons discussed above. Further, while the inventions at issue in cases such as Lilly were products *per se*, the holdings of those cases are also applicable to claims such as those at issue here since a disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

The rejection of claims 1-11, 14, 16, and 18-24 under 35 U.S.C. 112 first paragraph, for failing to comply with the enablement requirement, is maintained for the reasons stated in the Office Action of 5/17/07 and for the reasons set-forth below.

While being enabling for a method of predicting survival of a patient with gastric cancer comprising (a) detecting MN/CA IX polypeptide in a sample comprising gastric cancer tissue, (b) quantitating the level of said MN/CA IX polypeptide in said sample, (c) comparing the level of MN/CA IX polypeptide of step (b) to the average level of MN/CA IX polypeptide in analogous samples from subjects with gastric cancer, (d) determining that said patient has a prognosis of shorter survival than the average subject with gastric cancer if the level of MN/CA IX polypeptide level of step (b) is higher than the average level of MN/CA IX polypeptide in analogous samples from subjects with gastric cancer, does not reasonably provide enablement for a method which is prognostic for

every preneoplastic/neoplastic disease afflicting a subject vertebrate, wherein said disease affects a tissue, which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis, comprising (a) detecting MN/CA9 polypeptide in a preneoplastic/neoplastic tissue taken from said vertebrate, (b) quantitating the level of said MN/CA9 polypeptide in said sample, (c) comparing the level of MN/CA9 polypeptide of step (b) to the average level of MN/CA9 polypeptide in comparable samples taken from vertebrates afflicted by the same preneoplastic/neoplastic disease as the subject vertebrate, and (d) determining that said subject vertebrate has every type of poorer prognosis if the level of MN/CA9 polypeptide of step (b) is higher than the average level of MN/CA9 polypeptide in said comparable samples. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

In the Reply of 8/16/07, Applicant states that the burden of proof is upon the Examiner to challenge a presumptive enabling disclosure and that no evidence has been presented as to why the methods would not work as claimed. Applicant further argues that the diagnostic expression patterns of MN/CA IX have been established, that MN/CA IX is not just a tumor marker but is implicated in the progression of different tumor types, and Tockman 1992 is inapposite, as it relates to establishing endpoints to identify whether a biomarker is *diagnostically* useful for a particular tumor, not whether or not an established tumor biomarker is useful *prognostically*. Applicant further states that based on MN/CA IX's unique correlation with the presence of hypoxia and the value

of hypoxia in cancer prognosis in a broad range of tumors, renewed expression of MN/CA IX in tumor cells could signify hypoxia or tumor progression and corresponding poorer prognosis in diseases similar to gastric cancer (see lines 21-27 of page 42). Applicant further argues that Examiner has not provided any evidence that suggests that the claimed prognostic methods would not work for just any type of prognosis of preneoplastic/neoplastic diseases of tissues, where MN/CA IX is normally expressed but its expression is lost or diminished upon carcinogenesis.

The amendments to the claims and the arguments found in the Reply of 8/16/07 have been carefully considered, but are not deemed to be persuasive in regards to being enabled for methods which uses expression levels of MN/CA IX to determine every type of prognosis for every preneoplastic/neoplastic disease afflicting a subject vertebrate, wherein said disease affects a tissue, which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis. In regards to the argument that no evidence has been presented as to why the methods would not work as claimed, the Office Action of 5/17/07 states that factors to be considered in determining whether undue experimentation is required are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. These factors were addressed in the Office Action of 5/17/07,

which demonstrates that undue experimentation would be required to determine with any predictability that the method would function as claimed.

The Office Action of 5/17/07 contains the following text addressing why it would require undue experimentation by one of skill in the art to determine, with any predictability, that the broadly claimed methods for using MN/CA IX expression levels to determine every type of prognosis of every preneoplastic/neoplastic disease afflicting a subject vertebrate, wherein said disease affects a tissue, which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis would function as claimed:

"The specification teaches a method which is prognostic for a patient with gastric cancer comprising (a) detecting MN/CA 9 polypeptide in a sample comprising tissue from .... gastric cancer, (b) quantitating the level of said MN/CA 9 polypeptide in said sample, (c) comparing the level of MN/CA 9 polypeptide of step (b) to the average level of MN/CA 9 polypeptide in analogous ... samples from subjects with gastric cancer, (d) determining that said patient has a prognosis of shorter survival than the average subject with gastric cancer if the level of MN/CA 9 polypeptide level of step (b) is higher than the average level of MN/CA 9 polypeptide in analogous ... samples from subjects with gastric cancer...(see Example 2, Example 3, and Figure 5, in particular).

The level of unpredictability for providing any type of prognosis for any type of disease is quite high. The state of the prior art dictates that if a molecule such as MN/CA 9 polypeptide is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern in a particular tissue that would allow MN/CA 9 polypeptide to be used in a diagnostic or prognostic manner. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material

obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). Therefore, absent evidence of the polypeptide's expression in a particular tissue including the correlation to a diseased state, one of skill in the art would not be able to predictably use the polypeptide in any diagnostic or prognostic setting without undue experimentation.

Since neither the specification nor the prior art provide evidence of a universal association between the claimed method and ... every type of preneoplastic/neoplastic disease afflicting a subject vertebrate, wherein said disease affects a tissue, which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis ... every type of prognosis, a practitioner wishing to practice the claimed invention would be required to provide extensive experimentation to demonstrate such an association. Such experimentation would in itself be inventive.

Further, as noted in the written description rejection above, it is unclear which preneoplastic/neoplastic diseases affect a tissue which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis. Determining which preneoplastic/neoplastic diseases affect a tissue which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis would require undue experimentation.

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to a method which is prognostic for every preneoplastic/neoplastic disease afflicting a subject vertebrate, wherein said disease affects a tissue, which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis, comprising (a) detecting MN/CA9 polypeptide in just any sample comprising preneoplastic/neoplastic tissue taken from said vertebrate, (b) quantitating the level of said MN/CA9 polypeptide in said sample, (c) comparing the level of MN/CA9 polypeptide of step (b) to the average level of MN/CA9 polypeptide in just any "comparable" samples taken from vertebrates afflicted by the same preneoplastic/neoplastic disease as the subject vertebrate, and (d) determining that said subject vertebrate has every type of poorer prognosis if the level of MN/CA9 polypeptide of step (b) is higher than the average level of MN/CA9 polypeptide in said comparable samples, ... and Applicant has not enabled said method because it has not been shown that detecting MN/CA9 polypeptide in just any sample comprising preneoplastic/neoplastic tissue taken from just any vertebrate with just any preneoplastic/neoplastic disease, wherein said disease affects a tissue, which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis, quantitating the level of said

MN/CA9 polypeptide in said sample, comparing said level to the average level of MN/CA9 polypeptide in just any "comparable" samples taken from vertebrates afflicted by the same preneoplastic/neoplastic disease as the subject vertebrate, wherein said subject vertebrate has every type of poorer prognosis if the level of MN/CA9 polypeptide in the sample from said subject is higher than the average level of MN/CA9 polypeptide in said comparable samples...

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as claimed."

In regards to arguments that diagnostic expression patterns have been established for MN/CA IX, the instant claims are not drawn to diagnosis.

In regards to the argument that Tockman 1992 is inapposite, as it relates to establishing endpoints to identify whether a biomarker is *diagnostically* useful for a particular tumor, not whether or not an established tumor biomarker is useful *prognostically*, Tockman 1992 teaches a method that is used to identify diagnostic *and* prognostic markers. Tockman et al teaches that prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population trials (p. 2716s, col 2). A particular prognosis is a disease end point that is obviously amenable to the methods taught by Tockman et al.

Further, in regards to the theory that renewed expression of MN/CA IX in tumor cells could signify hypoxia or tumor progression and corresponding poorer prognosis in diseases similar to gastric cancer (see lines 21-27 of page 42), the claimed methods are drawn to *prognostic* methods based on MN/CA IX expression. How MN/CA IX may affect tumor progression or a particular prognosis is not claimed. Further, the unpredictability of said theory is highlighted in Pastorekov and Zavada, which teaches

that a subject with one cancer having a high MN/CA IX expression level would have the *opposite* prognosis as a patient with a different cancer that has a high MN/CA IX expression (see left column of page 251, in particular).

In regards to the argument that Examiner has not provided any evidence that suggests that the claimed prognostic methods would not work for just any type of prognosis of preneoplastic/neoplastic diseases of tissues, where MN/CA IX is normally expressed but its expression is lost or diminished upon carcinogenesis, it is noted that the specification discloses that "prognosis" encompasses survival, disease recurrence, and response to treatment (see page 9, in particular). Determining (1) which preneoplastic/neoplastic diseases affect a tissue which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis and (2) determining whether expression levels of MN/CA IX correlate with survival, disease recurrence, and response to treatment in subjects with preneoplastic/neoplastic diseases that affect a tissue which tissue normally expresses MN/CA IX protein, but loses or has significantly reduced MN/CA IX expression upon carcinogenesis would require undue experimentation.

Summary

No claim is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA

/Misook Yu/
Primary Examiner
Art Unit 1642